Remarks

Claims 1-2 and 5-7 are pending.

Status of claim 7

Claim 7 relates to a method that comprises detecting an expression profile of one or more colon cancer genes in a biological sample of a subject. That was true at the time the application was filed in 2004; it was true at the time of the restriction requirement in 2005, and remains true today. At no time has claim 7 been limited to the detection of polypeptides, as the Office action correctly observes. Claim 7 was included in the group of claims Applicants elected in response to the restriction requirement of 2005. Thus, Applicants have at all times during prosecution of this application been prosecuting the subject matter of claim 7. Applicants intend to continue to prosecute the subject matter of claim 7, which encompasses the detection of a nucleic acid. Applicants have argued the patentability of claim 7 separately from the patentability of claim 1 during prosecution and have never taken the position that claim 7 requires the detection of a polypeptide.

The Office action correctly identified that claim 7 is under examination and has not been withdrawn.

In view of Applicants' election of the subject matter of claims 1-8 in response to the restriction requirement of 2005, Applicants are entitled to pursue the subject matter of claim 7. Only a choice by Applicants to decline to pursue the subject matter of claim 7 could lead to claim 7 relating to non-elected subject matter. Applicants have never failed to pursue the subject matter of claim 7, which remains pending and presented for examination.

Rejections under 35 U.S.C. § 101

Claims 1, 2, and 5-7 stand rejected as allegedly unsupported by either a specific, substantial and credible utility or a well-established utility.

The utility of the claims is the utility recited in the preamble: diagnosing or monitoring colon cancer.

The utility is specific. Not all polypeptides (claims 1, 2, and 5-6) or genes (claim 7) are useful in diagnosing or monitoring colon cancer.

The utility is substantial. People die from colon cancer. Colon cancer can be treated if it is diagnosed. Treatment can be improved if the cancer can be monitored.

The utility is credible. With respect to claim 7, which relates to detection of gene expression, the Office action acknowledges that the application demonstrates that the GPR49 gene is overexpressed in colon cancer; the utility of claim 7 has therefore been demonstrated and the rejection should be withdrawn. With respect to claims 1-2 and 5-6, the Office action acknowledges that the overexpression of the mRNA in colon cancer "suggests a potential" for diagnosis using detection of the polypeptide (Office action, page 3). In discussing enablement, the Office action also appears to acknowledge that the overexpression of the mRNA in colon cancer provides a "reasonable basis" for concluding that differences in polypeptide levels would exist and would be diagnostically useful (Office action, page 7).

The Office action nevertheless argues that the claims lack a specific, substantial and credible utility because of a lack of direct evidence in the application that GPR49 protein is differentially expressed in colon cancer. Applicants submit that the Office action fails to apply the proper legal standard for utility. Compliance with the utility requirement does not require the presence of working examples, nor the presentation of proof that an asserted utility works as indicated. If a specific, substantial utility is asserted in an application, the utility need only be credible. The Office action acknowledges that the application provides reasonable bases for expecting the invention to work as asserted, even if no direct demonstration of protein overexpression is provided. In the context of medical treatment, the Manual of Patent Examining Procedure points out that "the asserted utility is usually clear—the invention is asserted to be useful in treating the particular disorder. If the asserted utility is credible, there is no basis to challenge such a claim on the basis that it lacks utility under 35 U.S.C. 101" (§ 2107.01(III), emphasis in original). Here, similarly, the asserted utility is clear—diagnosing or monitoring colon cancer. It is also credible, as the application provides a reasonable basis for concluding that the invention will work. The Office's quotation of caselaw to remind us that "a patent is not a hunting license" is not applicable here, as the application claims a very specific,

described utility based on the discovery that the GPR49 gene is overexpressed in colon cancer. The mere identification of a productive, focused path for further research is sufficient for utility. See, e.g., Manual of Patent Examining Procedure § 2107.01(III), quoting Cross v. Iizuka, 753 F.2d 1040, 1051 (Fed. Cir. 1985) ("Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility").

In view of the specific, substantial utility of diagnosis and monitoring of colon cancer and in view of the teachings in the application that make that utility credible, both in the context of detection of genes (claim 7) and of polypeptides (claims 1-2 and 5-6), Applicants respectfully request reconsideration and withdrawal of the rejections.

35 U.S.C. § 112, first paragraph

The Office action rejected claims 1-2 and 5-7 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Applicants request reconsideration and withdrawal of the rejection.

Claim 7

As Applicants have previously noted, claim 7 has never been limited to the use of GPR49 *polypeptides*; rather, the method of claim 7 uses the detection of an expression profile of one or more colon cancer *genes*, wherein one of said one or more colon cancer genes is GPR49. Although one could detect a GPR49 polypeptide when detecting an expression profile of a GPR49 gene, one could also detect a GPR49 nucleic acid. Applicants submit that the application provides direct evidence that the invention of claim 7 works as described. Indeed, there does not seem to be any serious disagreement that the application enables the invention of claim 7; the Office action merely asserts that the claim has been examined in the context of detecting a polypeptide. That is not a basis for a claim rejection. Applicants elected to prosecute claim 7. Claim 7 is therefore elected subject matter and under examination. Claim 7 does not require

detection of a polypeptide. The method of claim 7 is enabled. Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

Claims 1-2 and 5-6

Claims 1-2 and 5-6 are drawn to a method of diagnosing or monitoring colon cancer in a subject, comprising the steps of detecting a level of a GPR49 polypeptide in a biological sample of a subject and comparing said level to a control level of said GPR49 polypeptide, wherein the GPR49 polypeptide is over-expressed in colon cancer tissues as compared to disease-free colon tissues.

The Office action appears to acknowledge that the overexpression of GPR49 mRNA in colon cancer provides a "reasonable basis" for concluding that differences in GPR49 polypeptide levels would exist and would be diagnostically useful (Office action, page 7). The Office action nevertheless rejects the claims, arguing that an "invitation for further research and confirmation" does not constitute an enabling disclosure (Office action, page 7).

Applicants submit that the Office action is again applying an incorrect standard for patentability. "The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." Manual of Patent Examining Procedure § 2164.01, citing In re Angstadt, 537 F.2d 498, 504 (CCPA 1976). Applicants and the Office agree that the application provides a reasonable basis for concluding that differences in GPR49 polypeptide levels would exist and would be diagnostically useful. If the application provides a reasonable basis for expecting the invention to work, the enablement requirement has been satisfied. Some experimentation is acceptable, so long as it is not undue. Even if the GPR49 mRNA data were nothing more than an "invitation for further research and confirmation" by testing GPR49 protein levels in colon cancer to confirm that they are indeed elevated as predicted by the application, such is the nature of routine work in the art: the confirmatory assay would be focused (on GPR49 polypeptide levels in colon cancer) and could be performed using routine assays such as those referenced in the present application, assays that are therefore well within the level of skill in the art.

Because the application provides a reasonable basis for expecting the invention to work and because any experimentation would be routine and within the level of ordinary skill, Applicants respectfully request reconsideration and withdrawal of the rejections.

35 U.S.C. § 112, second paragraph

The Office action rejected claims 1-2 and 5-7 under 35 U.S.C. § 112, first paragraph, as allegedly indefinite for using "GPR49" as the sole means to identify the polypeptide (claims 1-2 and 5-6) or gene (claim 7) at issue. According to the Office action, "use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules" (Office action, page 8).

Applicants disagree with the rejection.

GPR49 is not a "laboratory designation." It is how "G protein-coupled receptor 49" is known in the art. The Office has, during prosecution, already identified publications in the art which identify the gene or protein as "GPR49." The term "GPR49" is very widely used in the art. The undersigned attorney is not aware that the art uses the term to refer to any gene or protein other than "G protein-coupled receptor 49." The Examiner's concern that the use of the term in the claim leads to confusion therefore appears to be unfounded. Furthermore, Applicants submit that the use of the term in the claim cannot be ambiguous because, read in view of the present application, "GPR49" could not be understood to refer to anything other than "G protein-coupled receptor 49."

Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Claims 1-2 and 5-7 are pending. Applicants respectfully request withdrawal of the outstanding rejection and allowance of the claims. Applicants invite the Examiner to call the undersigned attorney to address any remaining issues.

Respectfully submitted,

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